

Physiology of fluid and electrolyte responses during inactivity: water immersion and bed rest

JOHN E. GREENLEAF

Laboratory for Human Environmental Physiology, Biomedical Research Division, NASA,
Ames Research Center,
Moffett Field, CA 94035

ABSTRACT

GREENLEAF, JOHN E. Physiology of fluid and electrolyte responses during inactivity: water immersion and bed rest. *Med. Sci. Sports Exerc.*, Vol. 16, No. 1, pp. 20-25, 1984. This manuscript emphasizes the physiology of fluid-electrolyte-hormonal responses during the prolonged inactivity of bed rest and water immersion. An understanding of the total mechanism of adaptation (deconditioning) should provide more insight into the conditioning process. Findings that need to be confirmed during bed rest and immersion are: 1) the volume and tissues of origin of fluid shifted to the thorax and head; 2) interstitial fluid pressure changes in muscle and subcutaneous tissue, particularly during immersion; and 3) the composition of the incoming presumably interstitial fluid that contributes to the early hypervolemia. Better resolution of the time course and source of the diuretic fluid is needed. Important data will be forthcoming when hypotheses are tested involving the probable action of the emerging diuretic and natriuretic hormones, between themselves and among vasopressin and aldosterone, on diuresis and blood pressure control.

PLASMA VOLUME, INTERSTITIAL FLUID VOLUME, PLASMA ELECTROLYTES, DIURESIS, EXTRACELLULAR FLUID VOLUME, TOTAL BODY WATER

Human physical performance is limited by three major, but not necessarily independent, factors: substrate for muscular contraction, level of hyperthermia, and maintenance of consciousness (blood pressure). An important common denominator is water content and distribution, and the accompanying levels of electrolytes and protein. Blood, composed mainly of water, is the vehicle for delivery of oxygen to the tissues, for removal of metabolic end products, and for transfer of metabolic heat to the periphery. Henderson (38) has emphasized five physical properties of water that facilitate life and enhance survival potential in earthly organisms: 1) its power as the universal solvent; 2) its high thermal conductivity, which helps maintain cellular temperature constant; 3) its high latent heat of evaporation, which favors heat dissipation; 4) its high specific heat, which allows for the transfer of large quantities of heat with relatively small changes in body temperature; and 5) its dielectric constant, which allows for a high ionization potential.

Water, the largest single constituent in the human body, comprises 55-75% of body weight in a normal, healthy, 70-kg person; the average is about 61% (59). Total body water (TBW) is divided arbitrarily into that contained inside cells (intracellular water; 41% TBW or 29 liters) and that contained outside cells (extracellular water; 20% TBW or 14 liters). Extracellular water is further divided into that outside the vascular system (interstitial water; 16% TBW or 11.2 liters) and that inside the vascular system (plasma water; 4% TBW or 2.8 liters).

The plasma and interstitial fluid volumes provide the first line of defense against metabolic and environmental insult in order to protect intracellular homeostasis. Hence, the emphasis on understanding the physiology and dynamic interchange of fluid, electrolytes, and protein between these two compartments. Acute and chronic change of posture, the latter occurring with water immersion and bed rest, as well as increased levels of physical exercise, considered separately or in combination, result in large perturbations in extracellular fluid and electrolyte homeostasis.

This manuscript will suggest possible directions for future research and will refer to, but will not provide, an extensive review of the literature. Emphasis will focus on fluid and electrolyte shifts and balance during prolonged inactivity, that is, water immersion and bed rest. Understanding the process of deconditioning may provide insight into the conditioning adaptation syndrome.

WATER IMMERSION

Epstein (12) has reviewed the renal aspects of volume control during head-out immersion and annotated bibliographies of papers regarding physiological responses in mainly thermoneutral water have been prepared (34,46).

Any change in the gravitational force acting on the body causes an immediate shift in fluid and electrolytes with accompanying compensatory cardiorespiratory responses. Although data are few, probably the fastest re-

sponse is during rapid-onset head-to-foot ($+G_z$) acceleration where body fluid is translocated from the upper body to the legs and from the vascular system to the interstitial space (27,35,65). The dynamics of these fluid and electrolyte shifts have received relatively little attention and more research is needed.

An opposite and probably equally-rapid fluid-electrolyte response occurs during water immersion where the physiological responses are due to the hydrostatic pressure of the water on the skin, which is then translated to body tissues. This general increase in mechanical pressure on connective tissue is proportional to the depth of immersion, and the pressure on the abdomen pushes the diaphragm cephalad and results in compression of the thoracic cardiorespiratory structures. Heart size is increased by 30% within 6 s of immersion to the neck in vertical (standing) subjects (50,62). The volume of fluid shifted has been calculated (mean transit time through lungs \times cardiac output) from three subjects to be 700 ± 500 ml ($\bar{X} \pm SD$) (2). This measurement needs to be confirmed as it has been widely quoted and is the only datum available. Of the 700 ml, approximately 150 ml shifts into the heart. As a result, central venous (right atrial) and pulmonary arterial pressures increase from a control level of 2–4 mmHg to 13–16 mmHg (11,52,62). Intrathoracic (esophageal) pressure increases from -0.4 mmHg to $+3.4$ mmHg (11) and transmural pressure in the great veins increases from 3–5 mmHg to 12–15 mmHg (2,11). Venous pressure in the arm remains constant at about 4 mmHg while venous tone decreases from 17 to 12–13 mmHg \cdot ml $^{-1}$ \cdot 100 g $^{-1}$ tissue and remains depressed for at least 1 h after immersion is terminated (11). Systemic vascular resistance decreases by 30% ($\Delta = 5$ mmHg \cdot l $^{-1}$ \cdot min $^{-1}$) (2). Cardiac output increases by 32% in sitting immersion (2) and by 63% in standing immersion (22). There appears to be a more uniform distribution of pulmonary blood flow during immersion (61), which is similar to that occurring during short periods of weightlessness (55). Most of these cardiorespiratory responses are similar to those following a blood transfusion, and also mimic those occurring during negative pressure breathing; that is, breathing air from a tank at lower than atmospheric pressure (about -20.5 cm H $_2$ O) (1).

Simultaneously with the cephalic intravascular fluid shift, there is an absolute increase in plasma volume (hypervolemia) of 8–10% within the first 30 min (probably sooner) of immersion (31,41,53) and a progressive decline thereafter (31,32,33,41).

There is disagreement concerning the composition and source of the incoming fluid. Some data suggest the incoming fluid causes vascular hemodilution with reduction in hematocrit and the concentrations of hemoglobin and protein as well as the concentrations of the more readily diffusible plasma electrolytes (32,33,40,41). These results suggest that the composition of the incoming fluid was hypotonic (a lower osmolality) with respect to the existing plasma tonicity. On the other hand, when mildly-

dehydrated subjects were immersed, hypervolemia occurred with similar increases in Hct, Hb, RBC, protein, and albumin concentrations, but there were no significant changes in plasma sodium or osmotic concentrations (19,31). These responses suggest that the composition of the incoming fluid was isotonic in comparison with existing plasma tonicity. These results also depend upon the magnitude of the net influx and efflux of diffusible ions that become more important as diuresis increases and fluid and electrolytes are excreted.

The incoming fluid is probably derived from interstitial fluid. A relative decrease in capillary filtration and an increase in capillary reabsorption, resulting from the increased pressure on connective tissue from the immersion fluid, has been postulated by von Diringshofen (67). Accordingly, interstitial fluid pressure should increase during the first minutes of immersion when plasma volume increases and then decrease thereafter as plasma volume falls. Interstitial pressure has not been measured early during immersion, but Khosla and DuBois (41) found it decreases progressively from a control level of -0.5 ± 1.4 cm H $_2$ O in supine subjects in air, by -0.5 ± 0.3 , -1.2 ± 0.5 , and by -1.6 ± 0.8 cm H $_2$ O at 20, 40, and 60 min of head-out immersion, respectively. These important results are suggestive of at least a part of the mechanism for the changes in plasma volume, and point the way for future studies. Measurements of interstitial fluid composition, in conjunction with the volume shifts would be most interesting. Ascertaining the contribution of fluid from the intracellular compartment to this early plasma-interstitial fluid interaction would also be important, but more precise analytical techniques are required than are currently available.

In view of the relative state of general body hyperhydration induced as the result of immersion, the purpose for this hypervolemic response is not clear. It would appear to be a response to the connective tissues compression that perhaps reacts to a relatively lower plasma volume in the legs following the cephalad shift of fluid. This postulated imbalance of compression pressure might then be reflected in greater interstitial fluid pressure in the legs when compared with interstitial pressure elsewhere and fluid would be forced into the vascular system from the legs. Perhaps the hypervolemia is simply an anticipatory response to protect the plasma volume from the ensuing hypovolemia from the diuresis. However, this observed absolute increase in plasma volume should be confirmed before speculation is carried too far.

An in-depth review of the factors contributing to immersion diuresis has been published (12). It is generally agreed that the primary stimulus for the diuresis is the redistribution of blood into the thoracic region with an accompanying increase in central venous (right atrial and pulmonary arterial transmural) pressures. Accompanying the diuresis is a significant loss of sodium (natriuresis) which appears to be controlled independently from the diuresis (14,15,19,41), but may also contribute to the

magnitude of the diuresis by carrying water with the sodium ion. Stimuli from the atrial and pulmonary vascular structures, and perhaps elsewhere, initiate activation of various compensatory responses that induce diuresis to reduce the "excess" extracellular fluid. Some compensatory responses include increased renal prostaglandin activity (18), a decrease in sympathetic nervous stimulation of the kidney (6,23,24,39), a decrease in the activity of the renin-angiotensin-aldosterone system that promotes less kidney retention of sodium (7,16,20,21, 47) suppression of plasma vasopressin (anti-diuretic hormone) that allows less water reabsorption by the kidney (19,32,33), and the probable roles of natriuretic (8,9, 13,17,51,57,63,64) hormones. Many natriuretic substances and sodium transport (Na^+ , K^+ -ATPase) inhibitors, derived from extracts of brain, urine, plasma, and heart atrial tissue have been reported (8,9,63,64). The atrial and plasma natriuretic and plasma diuretic factors are in the process of being purified and it is uncertain at this time whether they are distinctly separate substances. A natriuretic factor has been isolated from heart atria from the rat, rabbit, dog, baboon, and humans (64) and possesses both natriuretic and diuretic properties (8,64). A diuretic factor has been isolated from dog plasma (36,43,44,45,60). Both factors appear to have an active component with molecular weight greater than 30,000 daltons (9,60), an active natriuretic component of less than 5,000 daltons (9), and an active diuretic component of less than 1,800 daltons (60). Elucidation of the interaction between the diuretic, antidiuretic, natriuretic, and anti-natriuretic hormones should prove to be very interesting.

BED REST

Annotated bibliographies of the physiological responses to prolonged bed rest in normal, healthy people have been prepared (28,34). Kozlowski (48) has reviewed the hypokinesia (bed rest) literature prior to 1969. We have prepared a more general review of the recent literature (29) as well as of the few data concerning the problem of changes in physical working capacity (peak oxygen uptake) during bed rest (30).

Prolonged bed rest induces general body dehydration. Assumption of the horizontal or slightly head-down (-6°) body positions results in a shift of fluid from the lower extremities to the thorax and head. Subjects experience fullness in the head and often report headache and nasal congestion. The volume of the thighs and legs decreases by about 900 ml (6%) (3), the lower legs by only 160 ml (5%), and calf circumference by 1 cm (2.7%) (37). Thus, the cephalic-fluid volume shift is derived in about equal proportions from the thighs and legs with about half as much fluid coming from subcutaneous tissue as from muscle and bone. As a result of the fluid shift, central venous pressure (heart and pulmonary area) increases ($^*P < 0.05$) from 5 to 7° cm H_2O (3), and interstitial fluid pressure

in the tibialis anterior muscle decreases from +4.6 to -2.8° mmHg and from +0.6 to -3.8° mmHg in subcutaneous leg tissue (37). A trend toward a more negative pressure would suggest a loss of fluid.

Plasma volume (calculated from changes in [Hb] and Hct) decreases by the second hour of horizontal bed rest by about 6.5% (68), by 4.3% (125 ml) after 6 h, and by 5.3% to 9.7% (150–300 ml) after 24 h (58,66). There are no data to determine whether plasma volume increases within the first 30 min of assumption of a recumbent position like that occurring with immersion. Hypovolemia is -10 to -13% (-350 to -450 ml) by the fourth day when isometric or isotonic exercise was performed for 1 h/d during bed rest, but plasma volume continued to decline when no exercise was performed (26) suggesting that exercise has a stabilizing effect on the rate of hypovolemia.

In comparison with the rate of hypovolemia, red-cell mass decreases more slowly; by 100 ml (5%) after 14 d of bed rest and by 300–550 ml after 30 d (42,56).

The interstitial volume decreases in the first few days of bed rest followed by a restoration to or an increase of 320 to 430 ml above control levels after 2 wk (26). The magnitude of this apparent overshoot was approximately equal to the volume of plasma lost (262–441 ml). Thus, after 14 d of bed rest the extracellular fluid volume (plasma plus interstitial) was unchanged from the ambulatory control level. It appears that maintenance of the extracellular volume takes precedence over maintenance of the plasma volume; the control appears to reside within the interstitial volume. These findings must be confirmed, and very important findings will come from simultaneous measurements of interstitial volume and pressure changes under conditions of inactivity and exercise.

There are few data on fluid volume levels beyond 2 wk of bed rest. Plasma volume continues to decrease and reaches -15% (-500 ml) after 20 d (26), -18% (-600 ml) at 70 d and -30% (-1000 ml) at 175 d (10). The extracellular volume remains at control levels after 175 d of bed rest due possibly to a larger compensatory increase in interstitial volume.

Total body water decreases by 3.4% (2900 ml) after 25 d of bed rest (49). Of this 2900-ml loss, 600–1000 ml (approximately one-third) were derived from plasma and the remaining two-thirds from the intracellular volume which includes the red-cell mass. These results suggest that control of body water distribution depends mainly on factors related to changes in hydrostatic pressure and, to a lesser extent, on the exercise (metabolic) duration and rate. A sufficient duration of heavy exercise performed intermittently during bed rest could probably maintain plasma volume near ambulatory control levels. This may be a technique for controlling the volume of interstitial fluid if the overshoot response occurs when plasma volume is not allowed to decrease. Significant edema may be the result with undesirable consequences,

particularly for astronauts with their "normal" cephalic edema.

Both lean body mass and fat content are lost during bed rest. A proportionately greater loss of fat than lean body mass occurs when isotonic exercise is performed (25). Thus, the loss of body weight during bed rest is partitioned between exercise-induced fat reduction and the loss of lean body mass resulting more from reduction in hydrostatic pressure and independent of metabolic rate.

In normally-hydrated subjects eating a controlled diet, the onset of diuresis and accompanying losses of sodium, potassium, and other osmols during bed rest is slower than during immersion and reaches a peak during the first 24 h (4,25,37). A second peak of urine sodium loss occurs about the fifth day and continues for at least nine additional days. Urine potassium excretion increases by 35% during the first hours of head-down bed rest and returns to control levels after 8 h (37). Potassium, like sodium, remains at control levels for 3 d and increased again from days 5-14 of bed rest (4,25).

The loss of plasma volume is accompanied by net changes of sodium and potassium that left the plasma concentrations of these ions unchanged from normal control levels (26,66). Plasma renin activity (PRA) and aldosterone concentration appear to increase somewhat during bed rest to probably counter sodium loss (4,37, 54,66) although this increase is not a consistent finding (5,28). Circadian changes in PRA may have influenced these results (54). Attenuation of plasma renin activity following an autotransfusion of blood suggests PRA was responding, at least in part, to the hypovolemia and perhaps to accompanying changes in blood pressure. A decrease in plasma aldosterone concentration would facilitate urine sodium loss and potassium retention; however, Chobanian et al. (5) observed no change in plasma aldosterone concentration during 3 wk of bed rest. If PRA and aldosterone are essentially constant after 3 d of bed rest, then another mechanism must be involved to account for the secondary natriuresis and kaliuresis begin-

ning after the fifth day. The actions of diuretic and natriuretic hormones are likely possibilities.

CONCLUSIONS AND RECOMMENDATIONS

With the exception of some water-immersion studies, most research on the process of deconditioning in humans has been of a descriptive nature. More such studies are needed that include:

1. Studying the effects of increasing duration and intensity of isometric and isotonic exercise during immersion and bed rest on responses of all physiological systems, but especially the vestibular, immune, thermoregulatory, and fluid-electrolyte systems.
2. Investigating the effects of circadian rhythm influences on hormonal function during bed rest and immersion.
3. More emphasis on events occurring during the first minutes of immersion and bed rest where physiological responses occur most rapidly.
4. And finally, more extensive investigation into various remedial procedures that can reduce or eliminate the adaptive (deconditioning) responses. Research study designs concerning remedial procedures must consider the separate effects of hypodynamia (reduced exercise levels) and hypogravia (reduced hydrostatic pressure) and their probable interaction.

The bed rest and immersion environments are good models for studying the more basic aspects of fluid volume and electrolyte physiology and their controlling humoral mechanisms. The function of the emerging diuretic and natriuretic hormones, on conjunction with vasopressin and the renin-angiotensin-aldosterone system, must contribute importantly in the metabolism of sodium which plays an important role in the etiology of blood pressure control, possibly orthostatic hypotension, and probably hypertension.

John E. Greenleaf is a Fellow of the American College of Sports Medicine.

REFERENCES

1. ACOSTONI, E., G. GURTNER, G. TORRI, and H. RAHN. Respiratory mechanics during submersion and negative pressure breathing. *J. Appl. Physiol.* 21:251-258, 1966.
2. ARBORELIUS, M., JR., U.I. BALDIN, B. LILJA, and C.E.G. LUNDGREN. Hemodynamic changes in man during immersion with the head above water. *Aerospace Med.* 43:592-598, 1972.
3. BLOMQUIST, C.G., J.V. NIXON, R.L. JOHNSON, JR., and J.H. MITCHELL. Early cardiovascular adaptation to zero gravity simulated by head-down tilt. *Acta Astronautica* 7:543-553, 1980.
4. CHAVARRI, M., A. GANGULY, J.A. LUETSCHER, and P.G. ZAGER. Effect of bedrest on circadian rhythms of plasma renin, aldosterone, and cortisol. *Aviat. Space Environ. Med.* 48:633-636, 1977.
5. CHOBANIAN, A.V., R.D. LILLE, A. TERCYAK, and P. BLEVINS. The metabolic and hemodynamic effects of prolonged bed rest in normal subjects. *Circulation* 59:551-554, 1974.
6. CLEMENT, D.L., C.L. PELLETER, and J.T. SHEPHERD. Role of vagal afferents in the control of renal sympathetic nerve activity in the rabbit. *Circ. Res.* 31:824-830, 1972.
7. CRANE, M.G. and J.J. HARRIS. Suppression of plasma aldosterone by partial immersion. *Metabolism* 23:359-368, 1974.
8. DEBOLD, A.J. and T.G. FLYNN. Cardionatrin I—a novel heart peptide with potent diuretic and natriuretic properties. *Life Sci.* 33:297-302, 1983.
9. DE WARDENER, H.E. and E.M. CLARKSON. The natriuretic hormone: recent developments. *Clin. Sci.* 63:415-420, 1982.
10. DONALDSON, C.L., S.B. HULLEY, D.E. MCMILLAN, R.S. HATTNER, and J.H. BAYERS. The effect of prolonged simulated non-gravitational environment on mineral balance in the adult male. *NASA Contractor Report* 108314, 1969, pp. 1-91.
11. ECHT, M., L. LANGE, and O.H. GAUER. Changes of peripheral venous tone and central transmural venous pressure during immersion in a thermo-neutral bath. *Pflügers Arch.* 352:211-217, 1974.
12. EPSTEIN, M. Renal effects of head-out water immersion in man: implications for an understanding of volume homeostasis. *Physiol. Rev.* 58:529-581, 1978.
13. EPSTEIN, M., N.S. BRICKER, and J.J. BOURGOIGNIE. Presence of a

- natriuretic factor in urine of normal men undergoing water immersion. *Kidney Int.* 13:152-158, 1978.
14. EPSTEIN, M., A.G. DENUNZIO, and M. RAMACHANDRAN. Characterization of renal response to prolonged immersion in normal man. *J. Appl. Physiol.* 49:184-188, 1980.
15. EPSTEIN, M., D.C. DUNCAN, and L.M. FISHMAN. Characterization of the natriuresis caused in normal man by immersion in water. *Clin. Sci.* 43:275-287, 1972.
16. EPSTEIN, M., L.M. FISHMAN, and H.B. HALE. Dissociation of aldosterone and 17-hydroxycorticosteroid (17-OHCS) release during water immersion in normal man. *Proc. Soc. Exp. Biol. Med.* 138:939-942, 1971.
17. EPSTEIN, M., J.L. KATSIKAS, and D.C. DUNCAN. Role of mineralocorticoids in the natriuresis of water immersion in man. *Circ. Res.* 37:228-236, 1973.
18. EPSTEIN, M., N.D. LIFSCHITZ, D.S. HOFFMAN, and J.H. STEIN. Relationship between renal prostaglandin E and renal sodium handling during water immersion in normal man. *Circ. Res.* 45:71-80, 1979.
19. EPSTEIN, M., S. PRESTON, and R.E. WEITZMAN. Isoosmotic central blood volume expansion suppresses plasma arginine vasopressin in normal man. *J. Clin. Endocrinol. Metab.* 52:256-262, 1981.
20. EPSTEIN, M., R. RE, S. PRESTON, and E. HABER. Comparison of the suppressive effects of water immersion and saline administration on renin-aldosterone in normal man. *J. Clin. Endocrinol. Metab.* 49:358-363, 1979.
21. EPSTEIN, M. and T. SARUTA. Effect of water immersion on renin-aldosterone and renal sodium handling in normal man. *J. Appl. Physiol.* 31:368-374, 1971.
22. FARHI, L.E. and D. LINNARSSON. Cardiopulmonary readjustments during graded immersion in water at 35°C. *Respir. Physiol.* 30:35-50, 1977.
23. GILMORE, J.P., S. ECHTENKAMP, C.R. WESLEY, and I.H. ZUCKER. Atrial receptor modulation of renal nerve activity in the nonhuman primate. *Am. J. Physiol.* 242(11):F592-F598, 1982.
24. GILMORE, J.P. and I.H. ZUCKER. The contribution of neural pathways to blood volume homeostasis in the subhuman primate. *Basic Res. Cardiol.* 75:281-288, 1980.
25. GREENLEAF, J.E., E.M. BERNAUER, L.T. JUHOS, H.L. YOUNG, J.T. MORSE, and R.W. STALEY. Effects of exercise on fluid exchange and body composition in man during 14-day bed rest. *J. Appl. Physiol.* 43:126-132, 1977.
26. GREENLEAF, J.E., E.M. BERNAUER, H.L. YOUNG, et al. Fluid and electrolyte shifts during bed rest with isometric and isotonic exercise. *J. Appl. Physiol.* 42:59-66, 1977.
27. GREENLEAF, J.E., P.J. BROCK, R.F. HAINES, S.A. ROSITANO, L.D. MONTGOMERY, and L.C. KEIL. Effect of hypovolemia, infusion, and oral rehydration on plasma electrolytes, ADH, renin activity, and +G_t tolerance. *Aviat. Space Environ. Med.* 48:693-700, 1977.
28. GREENLEAF, J.E., C.J. GREENLEAF, D. VAN DERVEER, and K.J. DORCHAK. Adaptation to prolonged bed rest in man: a compendium of research. *NASA Tech. Memo.* X-3307, 1976, pp. 1-180.
29. GREENLEAF, J.E. and S. KOZLOWSKI. Physiological consequences of reduced physical activity during bed rest. *Exerc. Sport Sci. Rev.* 10:84-119, 1982.
30. GREENLEAF, J.E. and S. KOZLOWSKI. Reduction in peak oxygen uptake after prolonged bed rest. *Med. Sci. Sports Exerc.* 14:477-480, 1982.
31. GREENLEAF, J.E., J.T. MORSE, P.R. BARNES, J. SILVER, and L.C. KEIL. Hypervolemia and plasma vasopressin response during water immersion in men. *J. Appl. Physiol.* 55:1688-1693, 1983.
32. GREENLEAF, J.E., E. SHVARTZ, and L.C. KEIL. Hemodilution, vasopressin suppression, and diuresis during water immersion in man. *Aviat. Space Environ. Med.* 52:329-336, 1981.
33. GREENLEAF, J.E., E. SHVARTZ, S. KRAVICK, and L.C. KEIL. Fluid shifts and endocrine responses during chair rest and water immersion in man. *J. Appl. Physiol.* 48:79-88, 1980.
34. GREENLEAF, J.E., L. SILVERSTEIN, J. BLISS, V. LANGENHEIM, H. ROSSOW, and C. CHAO. Physiological responses to prolonged bed rest and fluid immersion in man: a compendium of research (1974-1980). *NASA Tech. Memo.* 81324, 1982, pp. 1-110.
35. GREENLEAF, J.E., H.O. STINNETT, G.L. DAVIS, J. KOLLIAS, and E.M. BERNAUER. Fluid and electrolyte shifts in women during +G_t acceleration after 15 days' bed rest. *J. Appl. Physiol.* 42:67-73, 1977.
36. GUPTA, B.N., R.J. LINDEN, D.A.S.G. MARY, and D. WEATHERILL. The diuretic and natriuretic responses to stimulation of left atrial receptors in dogs with different blood volumes. *Q. J. Exp. Physiol.* 67:235-258, 1982.
37. HARGENS, A.G., C.M. TIPTON, P.D. GOLLNICK, S.J. MUBARAK, B.J. TUCKER, and W.H. AKESON. Fluid shifts and muscle function in humans during acute simulated weightlessness. *J. Appl. Physiol.* 54:1003-1009, 1983.
38. HENDERSON, L.J. *The Fitness of the Environment*. Boston: Beacon Press, 1958, pp. 1-317.
39. KARIM, F., C. KIDD, C.M. MALPUS, and P.E. PENNA. The effects of stimulation of the left atrial receptors on sympathetic efferent nerve activity. *J. Physiol. (Lond.)* 227:243-260, 1972.
40. KHOSLA, S.S. and A.B. DUBOIS. Fluid shifts during initial phase of immersion diuresis in man. *J. Appl. Physiol.* 46:703-708, 1979.
41. KHOSLA, S.S. and A.B. DUBOIS. Osmoregulation and interstitial fluid pressure changes in humans during water immersion. *J. Appl. Physiol.* 51:686-692, 1981.
42. KIMZEY, S.L., J.T. LEONARD, and P.C. JOHNSON. A mathematical and experimental simulation of the hematological response to weightlessness. *Acta Astronautica* 6:1289-1303, 1979.
43. KNAPP, M.F., R.J. LINDEN, and M.J. PEARSON. Diuresis from stimulation of left atrial receptors: ADH and the Malpighian tubules of *Rhodnius prolixus*. *Q. J. Exp. Physiol.* 66:333-338, 1981.
44. KNAPP, M.F., R.J. LINDEN, M.J. PEARSON, and J.M. PITHER. Abolition of atrial receptor diuresis and of release of humoral agent by cooling the vagal nerves. *Q. J. Exp. Physiol.* 68:179-188, 1983.
45. KNAPP, M.F., R.J. LINDEN, M.J. PEARSON, J.M. PITHER, and E.M. WHITAKER. Diuresis from stimulation of left atrial receptors: initial purification steps from plasma of the causative agent. *Q. J. Exp. Physiol.* 66:439-445, 1981.
46. KOLLIAS, J., D. VAN DERVEER, K.J. DORCHAK, and J.E. GREENLEAF. Physiologic responses to water immersion in man: a compendium of research. *NASA Tech. Memo.* X-3308, 1976, pp. 1-87.
47. KORZ, R., F. FISCHER, and C. BEHN. Renin-angiotensin system in simulated hypervolemia induced by immersion. *Klin. Wochenschr.* 47:1263-1268, 1969.
48. KOZLOWSKI, S. Fizjologiczne skutki hipokinezy. (Physiological effects of hypokinesia.) *Postępy Astronautyki* 7:25-47, 1969.
49. KROTOV, V.P., A.A. TITOV, YE. A. KOVALENKO, V.V. BOGOMOLOV, L.L. STAZHADZE, and V.P. MASENKO. Changes in fluid metabolism during prolonged hypokinesia with the body in antithrostatic position. *Kosm. Biol. Aviakosm. Med.* 11:32-37, 1977.
50. LANGE, L., S. LANGE, M. ECHT, O.H. GAUER, and H. DANNENBERG. Heart volume in relation to body posture and immersion in a thermoneutral bath. *Pflügers Arch.* 352:219-226, 1974.
51. LINKENBACH, H.J., P. ECKERT, and O.H. GAUER. Nachweis eines diuretischen Faktors in menschlichen Serum während der durch Expansion des intrathorakalen Blutvolumens ausgelösten Diurese. *Pflügers Arch.* 293:107-114, 1967.
52. LOLLGEN, H., G. NIEDING, K. KOPPEHAGEN, F. KERSTING, and H. JUST. Hemodynamic response to graded water immersion. *Klin. Wochenschr.* 59:623-628, 1981.
53. MCCALLY, M. Plasma volume response to water immersion: implications for space flight. *Aerospace Med.* 35:130-132, 1964.
54. MELADA, G.A., R.H. GOLDMAN, J.A. LUETSCHER, and P.G. ZAGER. Hemodynamics, renal function, plasma renin, and aldosterone in man after 5 to 14 days of bedrest. *Aviat. Space Environ. Med.* 46:1049-1055, 1975.
55. MICHELS, D.B. and J.B. WEST. Distribution of pulmonary ventilation and perfusion during short periods of weightlessness. *J. Appl. Physiol.* 45:987-998, 1978.
56. MILLER, P.B., R.L. JOHNSON, and L.E. LAMB. Effects of moderate physical exercise during four weeks of bedrest on circulatory functions in man. *Aerospace Med.* 36:1077-1082, 1965.
57. MYERS, J.W. and J.A. GODLEY. Cardiovascular and renal function during total body water immersion of dogs. *J. Appl. Physiol.* 22:573-579, 1967.
58. NIXON, J.V., R.G. MURRAY, C. BRYANT, et al. Early cardiovascular adaptation to simulated zero gravity. *J. Appl. Physiol.* 46:541-548, 1979.
59. OSER, B.J. (Ed.). *Hawk's Physiological Chemistry*. New York: McGraw-Hill, 1965, pp. 1-1472.
60. PITHER, J.M., M.F. KNAPP, R.J. LINDEN, and M.J. PEARSON. Diuresis from stimulation of left atrial receptors in dogs: further purification of the causative agent from plasma. *Q. J. Exp. Physiol.* 68:167-177, 1983.

FLUID AND ELECTROLYTE RESPONSES DURING INACTIVITY

61. RENNIE, D.W., P. DI PRAMPERO, and P. CERRETELLI. Cardiac output of man in water. In: *Proceedings of the XXIV International Union Physiol. Sci.* Washington, DC: 1968, p. 364.
62. RISCH, W.D., H.-J. KOUBENEK, O.H. GAUER, and S. LANGE. Time course of cardiac distension with rapid immersion in a thermo-neutral bath. *Pflügers Arch.* 374:119-120, 1978.
63. THIBAUT, G., R. GARCIA, M. CANTIN, and J. GENEST. Atrial natriuretic factor. Characterization and partial purification. *Hypertension* 5:Suppl. 1:1-75-1-80, 1983.
64. TRIFFODO, N.C., A.A. MACPHEE, and F.E. COLE. Partially purified human and rat atrial natriuretic factor. *Hypertension* 5:(suppl.) 1:1-81-1-88, 1983.
65. VAN BEAUMONT, W., J.E. GREENLEAF, H.L. YOUNG, and L. JUHOS. Plasma volume and blood constituent shifts during +G_i acceleration after bed rest with exercise conditioning. *Aerospace Med.* 45:425-430, 1974.
66. VOLICER, L., R. JEAN-CHARLES, and A.V. CHOBANIAN. Effects of head-down tilt on fluid and electrolyte balance. *Aviat. Space Environ. Med.* 47:1065-1068, 1976.
67. VON DIRINGSHOFEN, H. Die Wirkungen des hydrostatischen Druckes des Wasserbades auf den Blutdruck in den Kapillaren und die Bindegewesbsentwässerung. *Z. Kreislauf.* 37:382-390, 1948.
68. WIDDOWSON, E.M. and R.A. MCCANCE. The effect of rest in bed on plasma volume as indicated by haemoglobin and haematocrit levels. *Lancet* 1:539-540, 1950.